A Role for Social and Behavioral Sciences in Genomic Translation: Making Room at the Table

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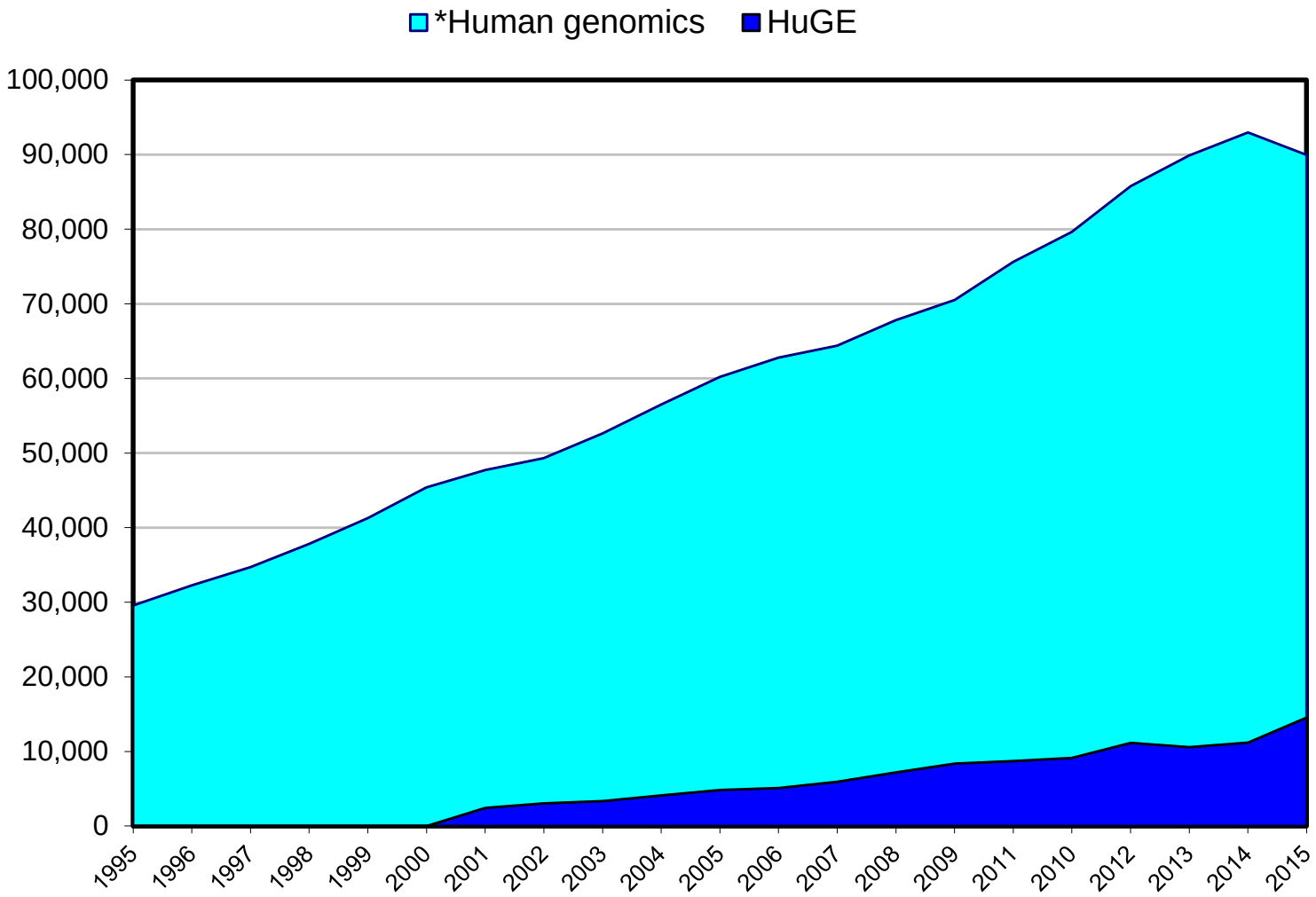
Today's talk

- Notes from the field approach
- Who's at the genomic translation table & why?
- Obligation to reduce health disparities is an optimal collaboration nexus for genomic translation
- Borrowed recommendations

Publications related to genetics:



PubMed query “gene OR genetic OR genome OR genomic” / limited to human vs. HuGE Navigator, Sep 2016

High Profile Genomics Initiatives

All of Us℠ | The Precision Medicine Initiative®

THE FUTURE OF HEALTH BEGINS WITH YOU

Evaluation of Genomic Applications in Practice & Prevention (EGAPP)

Table. Evidence-based Classification of Genomic Tests and Family Health History

Tier	Definition	Example(s)
1	Implementation in practice is supported by a base of synthesized evidence.	*BRCA*-associated hereditary breast and ovarian cancer (U.S. Preventive Services Task Force B recommendation); Lynch syndrome (EGAPP)
2	May provide information for informed decision making based on existing evidence; however, synthesized evidence is insufficient to support routine implementation in practice.	Family health history in primary care, with few exceptions
3	Not ready for routine implementation in practice based on synthesized evidence culminating in recommendations against use, OR no relevant synthesized evidence identified.	Direct-to-consumer personal genomic tests

https://www.cdc.gov/egappreviews/about.html

Basic Genomic Science

Social & Behavioral Science

neither here

nor there

Epidemiology, Data Science & Clinical Practice

Not Invited to the Banquet

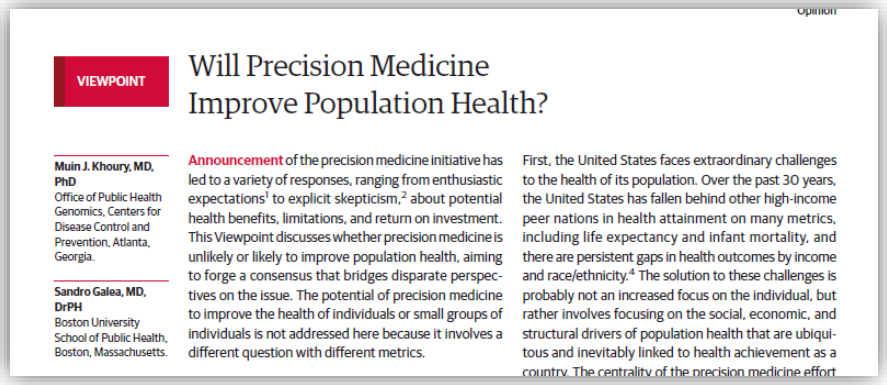
- Focus Group Discussions with SBM members (N=40)
- 90-minute video conferencing

- Difficult to find collaborators in epidemiology & clinical sciences
- Lack of funding incentives for social and behavioral science
- Few opportunities for cross disciplinary discussions

Report to Soc Beh Med, Executive Committee, April, 2018; McBride, Allen, Arredondo, Guan, Kaphingst, Klein, Wang,

Social & Behavioral Scientists Slow to Engage in Genomics

1. Concern that genomics will eclipse social determinants of health
2. Infeasible to disseminate high tech & expensive genomic applications
3. Genomic applications unlikely to improve health promotion interventions



VIEWPOINT

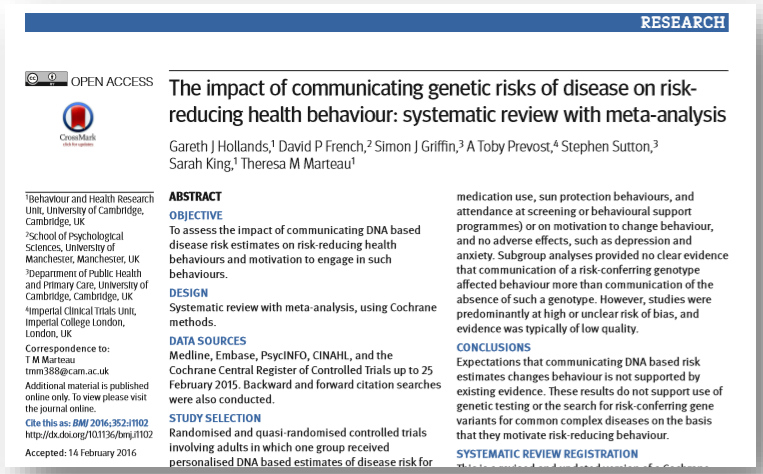
Will Precision Medicine Improve Population Health?

Muin J. Khoury, MD, PhD
Office of Public Health Genomics, Centers for Disease Control and Prevention, Atlanta, Georgia.

Sandro Galea, MD, DrPH
Boston University School of Public Health, Boston, Massachusetts.

Announcement of the precision medicine initiative has led to a variety of responses, ranging from enthusiastic expectations[1] to explicit skepticism,[2] about potential health benefits, limitations, and return on investment. This Viewpoint discusses whether precision medicine is unlikely or likely to improve population health, aiming to forge a consensus that bridges disparate perspectives on the issue. The potential of precision medicine to improve the health of individuals or small groups of individuals is not addressed here because it involves a different question with different metrics.

First, the United States faces extraordinary challenges to the health of its population. Over the past 30 years, the United States has fallen behind other high-income peer nations in health attainment on many metrics, including life expectancy and infant mortality, and there are persistent gaps in health outcomes by income and race/ethnicity.[4] The solution to these challenges is probably not an increased focus on the individual, but rather involves focusing on the social, economic, and structural drivers of population health that are ubiquitous and inevitably linked to health achievement as a country. The centrality of the precision medicine effort



RESEARCH

OPEN ACCESS

The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis

Gareth J Hollands,[1] David P French,[2] Simon J Griffin,[3] A Toby Prevost,[4] Stephen Sutton,[3] Sarah King,[1] Theresa M Marteau[1]

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[2]School of Psychological Sciences, University of Manchester, Manchester, UK
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Additional material is published online only. To view please visit the journal online.
Cite this as: *BMJ* 2016;352:i1102
http://dx.doi.org/10.1136/bmj.i1102
Accepted: 14 February 2016

ABSTRACT

OBJECTIVE
To assess the impact of communicating DNA based disease risk estimates on risk-reducing health behaviours and motivation to engage in such behaviours.

DESIGN
Systematic review with meta-analysis, using Cochrane methods.

DATA SOURCES
Medline, Embase, PsycINFO, CINAHL, and the Cochrane Central Register of Controlled Trials up to 25 February 2015. Backward and forward citation searches were also conducted.

STUDY SELECTION
Randomised and quasi-randomised controlled trials involving adults in which one group received personalised DNA based estimates of disease risk for

medication use, sun protection behaviours, and attendance at screening or behavioural support programmes) or on motivation to change behaviour, and no adverse effects, such as depression and anxiety. Subgroup analyses provided no clear evidence that communication of a risk-conferring genotype affected behaviour more than communication of the absence of such a genotype. However, studies were predominantly at high or unclear risk of bias, and evidence was typically of low quality.

CONCLUSIONS
Expectations that communicating DNA based risk estimates changes behaviour is not supported by existing evidence. These results do not support use of genetic testing or the search for risk-conferring gene variants for common complex diseases on the basis that they motivate risk-reducing behaviour.

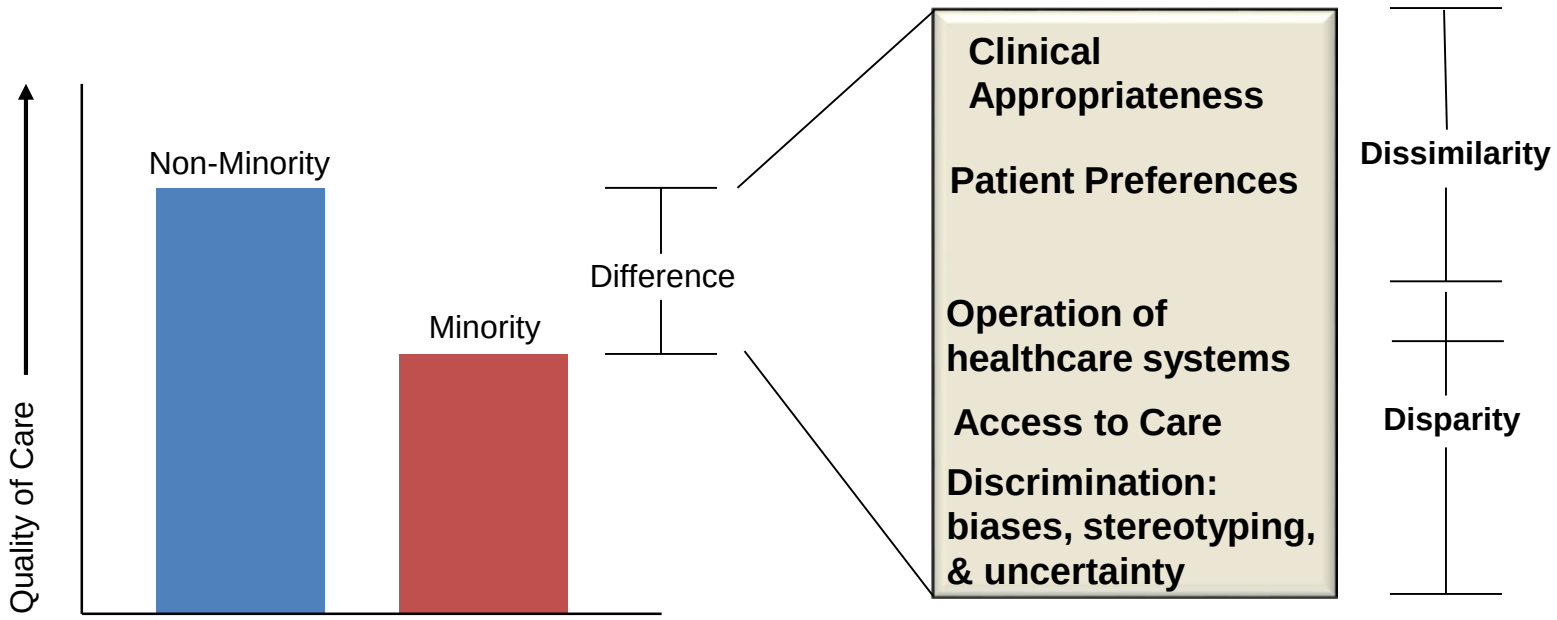
SYSTEMATIC REVIEW REGISTRATION

McBride, Transl Beh Med, 2018;

What is a collaboration nexus where everybody wins!

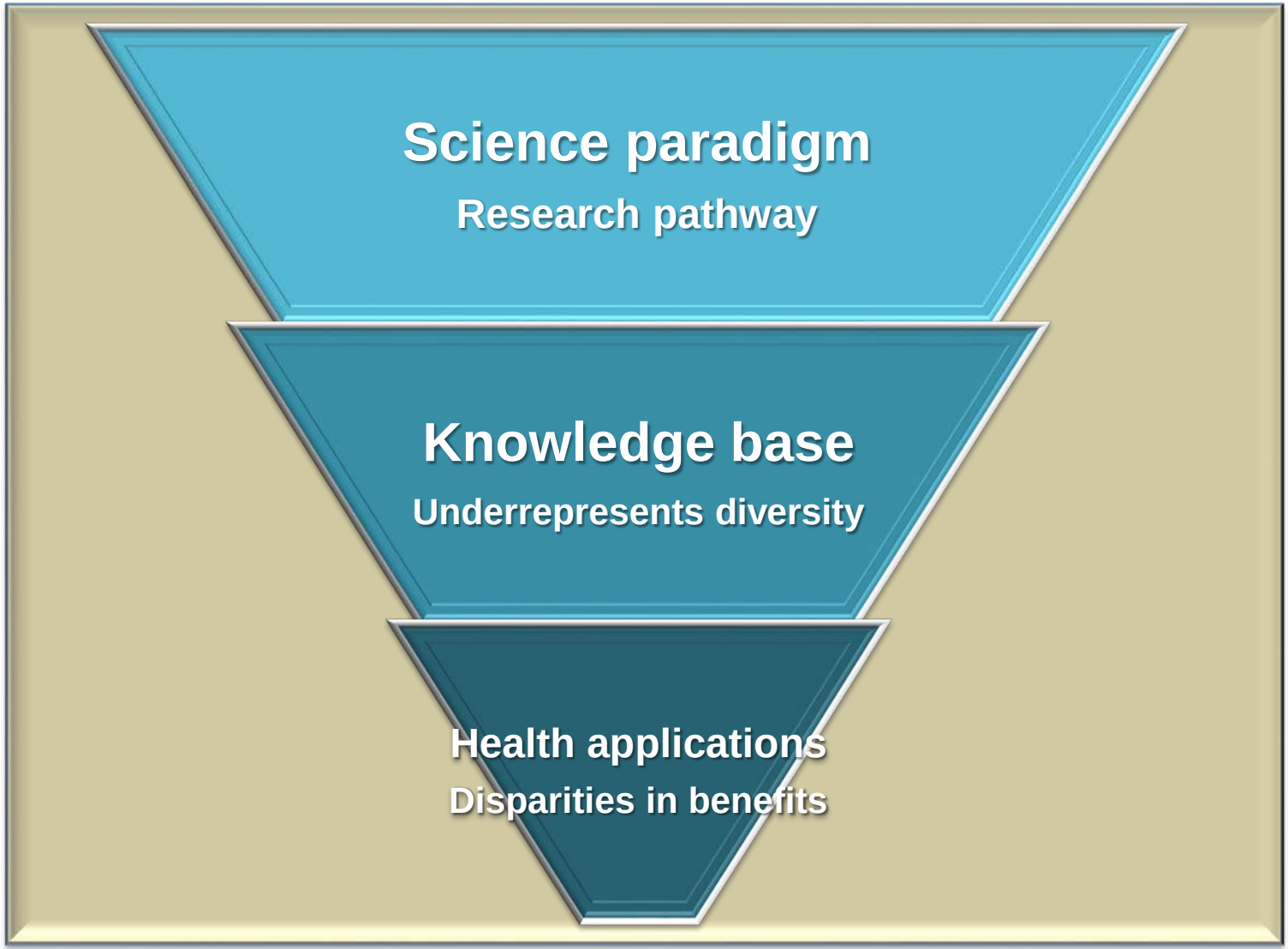
Model of Health Care Disparities

Not all dissimilarities in care are necessarily a disparity.



Source: Gomes, C. and McGuire T.G. 2001. Identifying the sources of racial and ethnic disparities in health care use. Unpublished manuscript cited in: IOM,. 2002. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*. Smedley, B., A. Stith and A. Nelson, eds. Washington DC: National Academy Press

Layers of Influence on Disparities Related to Genomic Translation

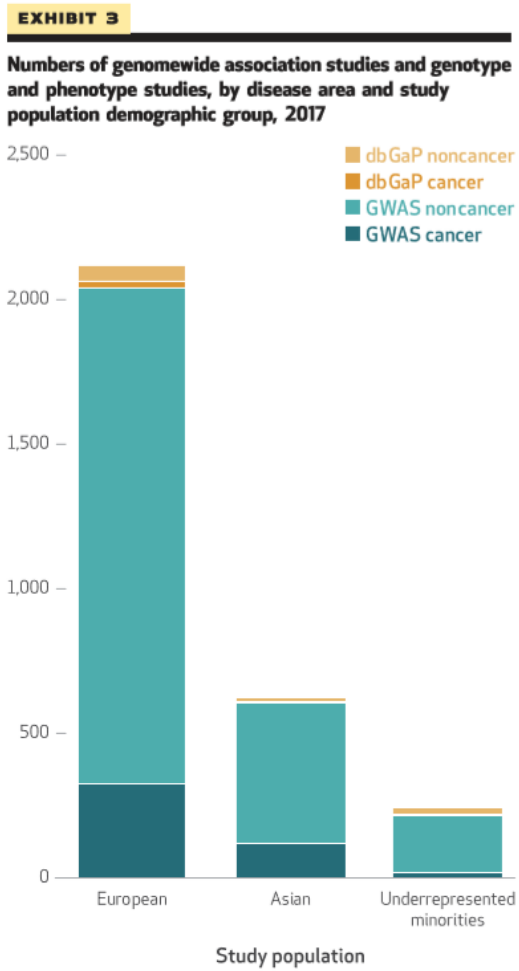


Accepted Translation Paradigm

- **Stage 1:** Basic Research
- **Stage 2:** Treatment Development
- **Stage 3:** Efficacy
- **Stage 4:** Effectiveness
- **Stage 5: Adaptation to real world**

T1	T2	T3	T4
From Gene Discovery to Health Application	From Health Application to Evidence-based Guideline	From Guideline to Health Practice	From Practice to Health Impact

Knowledge Based on European Ancestry Groups



Landry et al., 2018

- **Risk-allele frequencies modest correlations between ancestry groups**
- **Effect sizes varied:**
  - Particularly for European vs. African groups
  - Some in opposite direction
  - Same direction but differed by 2-fold

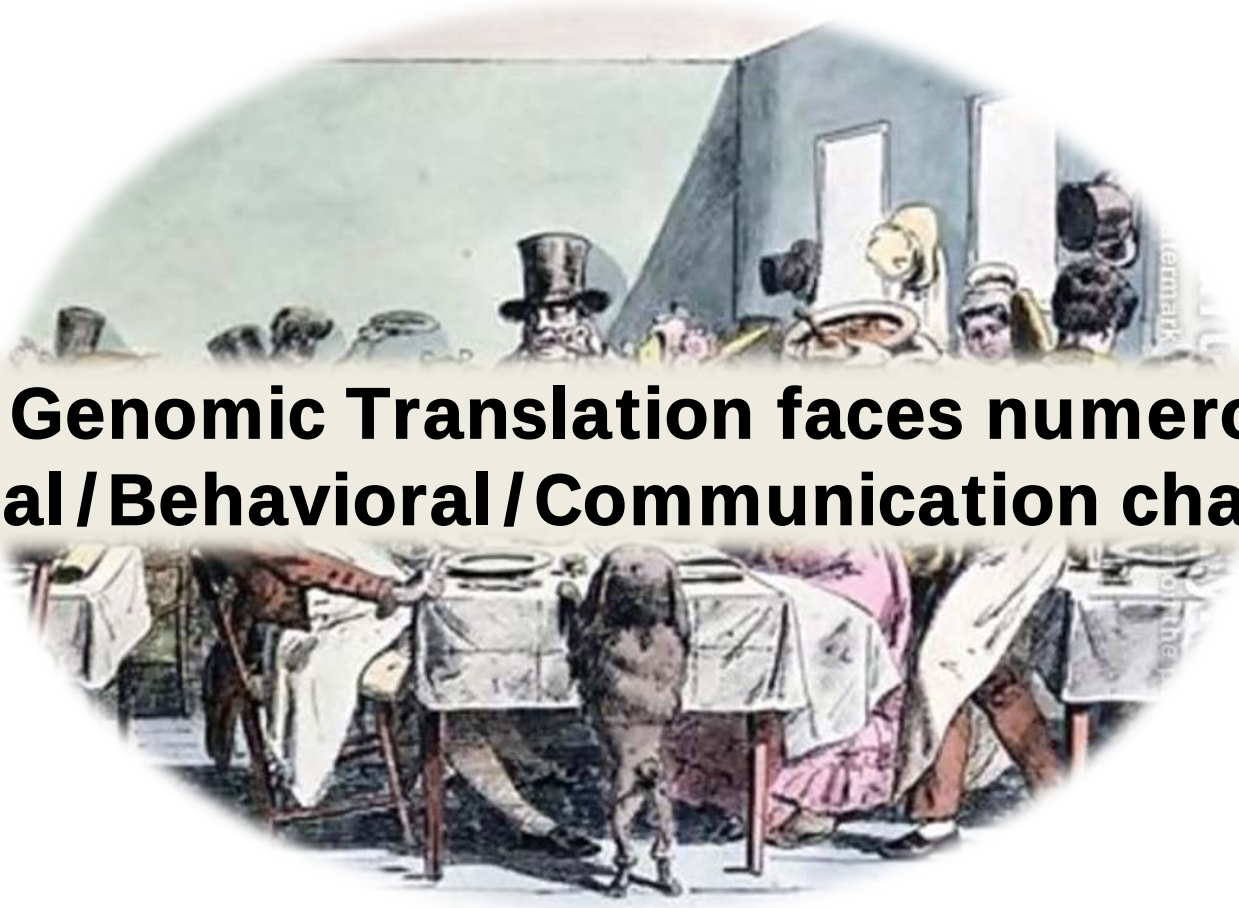
Ntzani et al., Hum Genet, 2012

Health Application: HBOC Genetic testing

- **GWAS (59 studies) 5% "underrepresented minorities"**
- **Inadequate risk models**
  - High risk white families
- **Understanding of testing benefits**
  - Based on European Ancestry (BRCA -- Ashkenazi populations)
- **Estimating population prevalence**
  - High rates of uncertain significance & novel deleterious mutations among African Americans

Hall & Olopade, 2006
Landry et al., 2018

Back at the banquet…



Genomic Translation faces numerous Social / Behavioral / Communication challenges

Recruitment & uptake of genetic services: Social/Behavioral/Communication challenges

- **What do communities of color have to gain from research participation?**
  - What is lost if they do not participate?
- **Comprehension of testing results and appropriate follow-up?**
- **Decision support for those at high risk**
- **Family communication about risk**

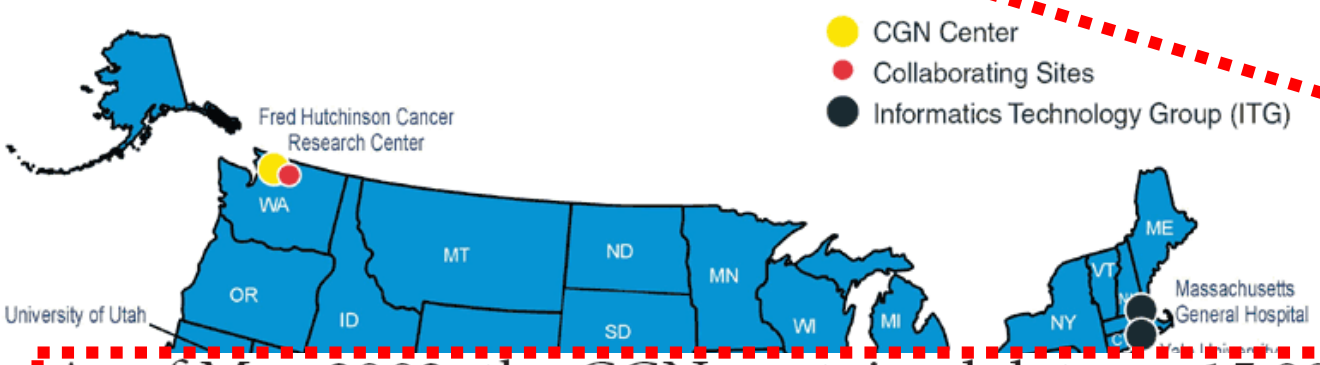
Introduction

Community Genetics

Community Genet 2008;11:191–192
DOI: 10.1159/000116877

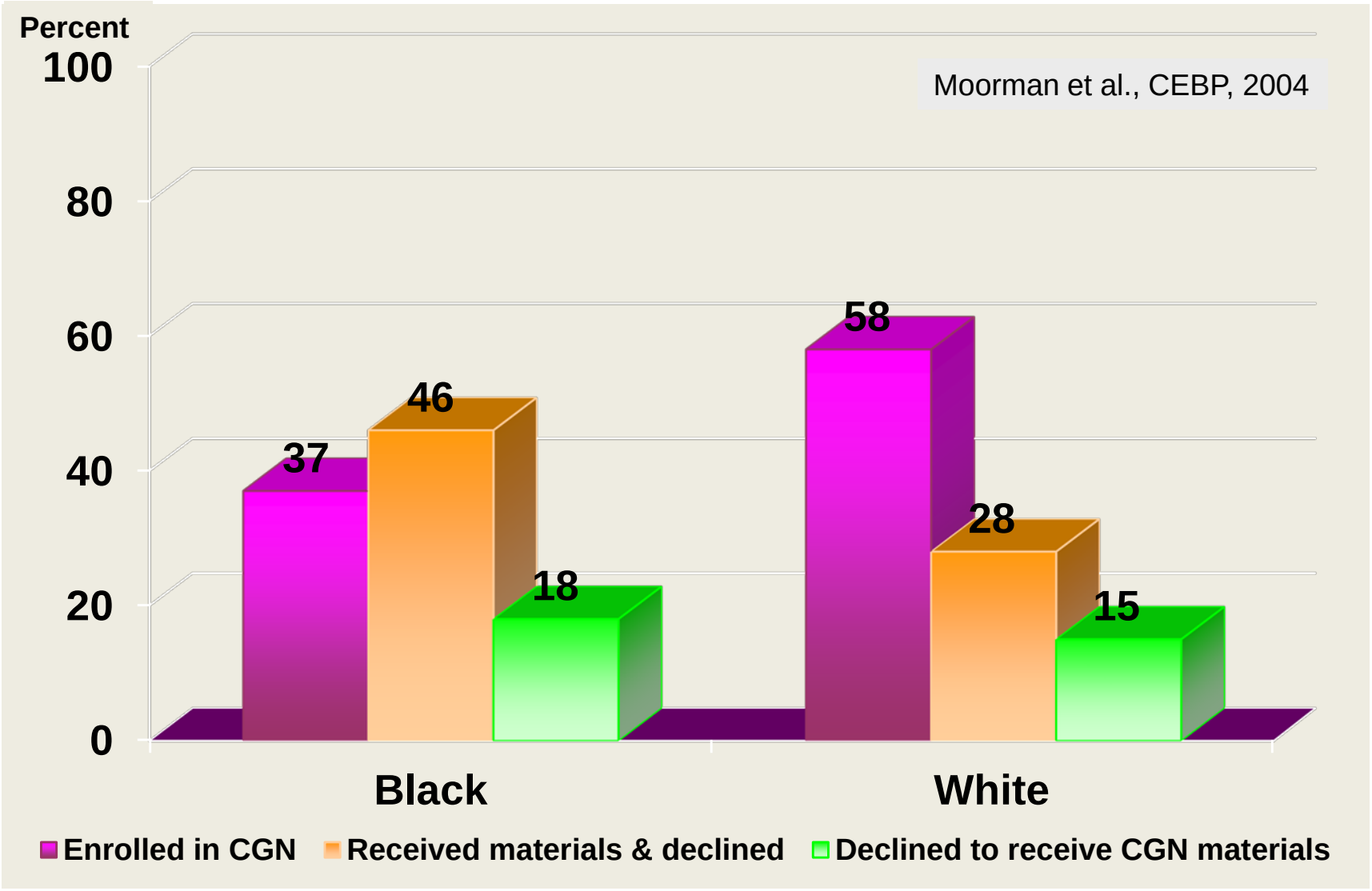
Increasing Minority Participant Enrollment into a Cancer Family Registry: The Cancer Genetics Network

Deborah J. Bowen[d] Thuy Vu[a, b] Carol Kasten-Sportes[c]



As of May 2002, the CGN contained data on 15,007 participants and 241,948 family members. The majority of CGN participants were of Non-Hispanic White/Caucasian ethnicity (90%), with few numbers of Hispanic (4%), Black (3%), Asian (1%), and other ethnicities (2%). These participation figures did not match those of the general public, nor did they match the catchment areas of the participating sites in the CGN.

Minority recruitment to CGN



- **Observational study**
- **NCI-funded Cancer Research Network**
  - Henry Ford Health System clinical recruitment site
- **Multiplex genetic test for 8 common health conditions**
  - Removed access barriers
- **Sample: Healthy adults** (25-40/ without health condition)

Multiplex Testing Uptake

	Gender (Men vs. Women) Adjusted+ OR (95% CI)	**Education** (Low vs. High) Adjusted+ OR (95% CI)	**Race** (AA vs. White) Adjusted+ OR (95% CI)
Baseline survey	.65 (0.58,0.72)**	0.86 (0.79,0.97)*	0.88 (0.80, 0.99)*
Visited website	.81 (0.67, 0.99)*	1.07 (0.88, 1.32)	0.52 (0.43,0.63)**
Tested	1.02 (0.73, 1.42)	0.80 (0.57, 1.11)	0.36 (0.25,0.50)***

+adjusted for other two categories

Alford et. al. Public Health Genomics, 2010

All of Us: Recruitment

NIH National Institutes of Health
All of Us Research Program

National Network of Inaugural Partners

National Partners

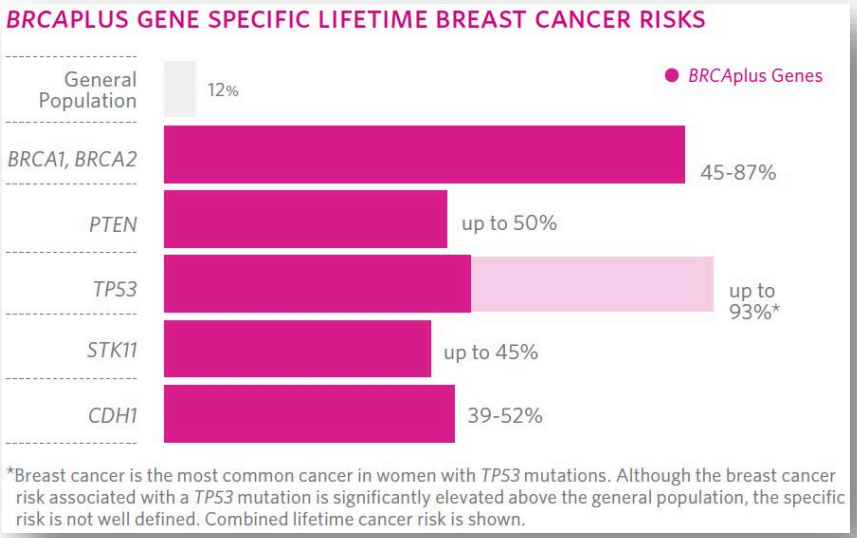
Regional Medical Centers

FQHCs

Community Partners

Health Applications

Genetic testing

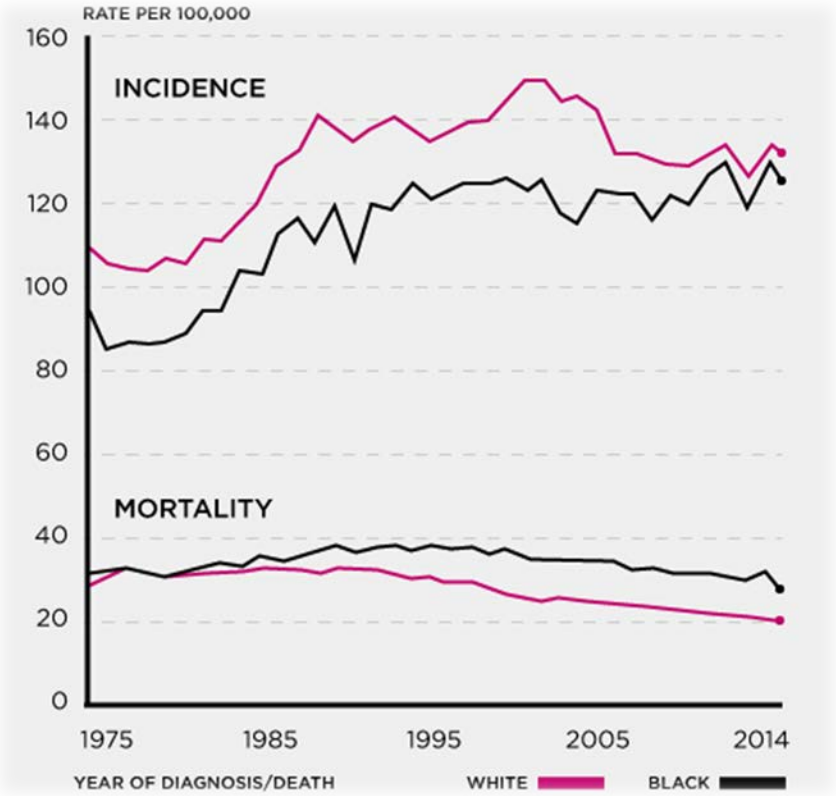


Life saving options

- **Enhanced screening**
- **Risk-reducing surgery**
- **Chemoprevention**
  - Tamoxifen
  - Oral contraceptives
- **Family member benefits**

Health Applications con.

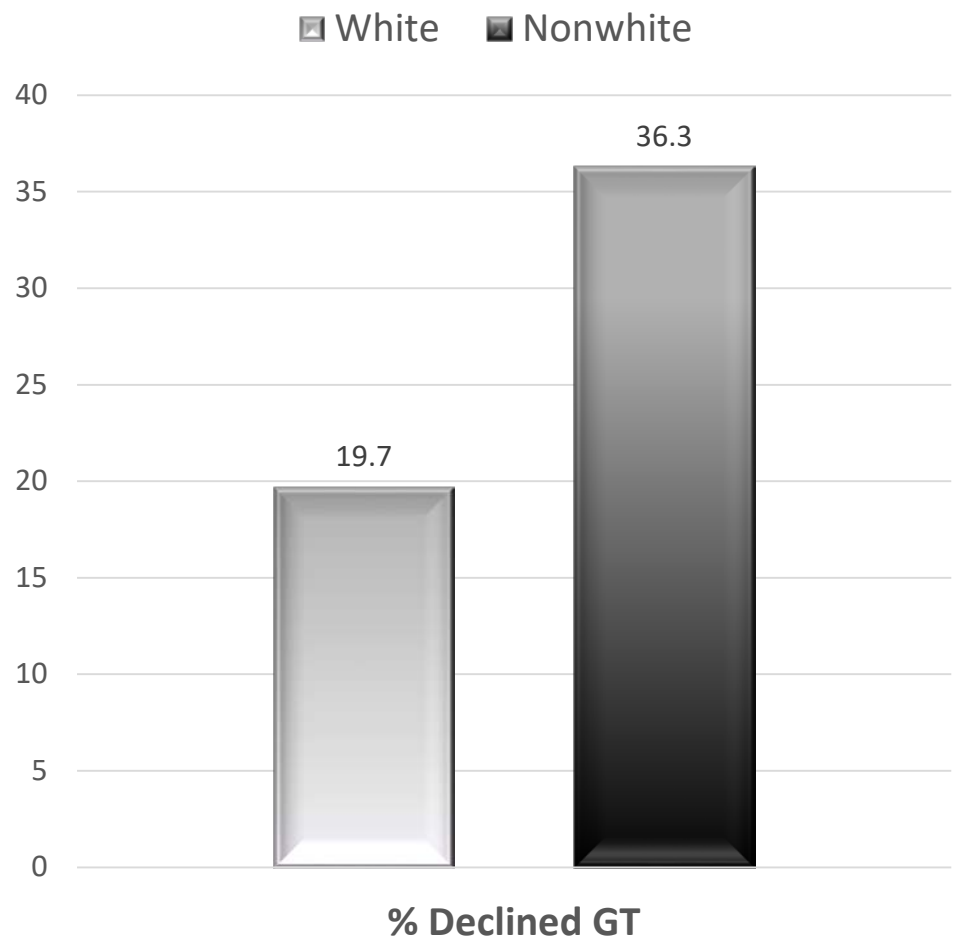
Identifying & Offering Genetic Testing to Cancer Patients



- **Tumor registries to identify probands**
  - Tertiary specialty centers
  - Over-represents white & high SES
- **Efforts to increase reach**
  - Few efforts at community engagement
  - Telegenetics

Declined genetic testing by race

- Used outreach approaches to increase reach
- DC site: 13.6 (n=91) “nonwhite”
- Whites 2x more likely to undergo genetic testing (Butrick)
- New Mexico trial cite 5.8% were hispanic or “nonwhite” (Kinney, 2014)



Butrick et al., 2015

Uptake of genetic testing by genetic counseling approach & race

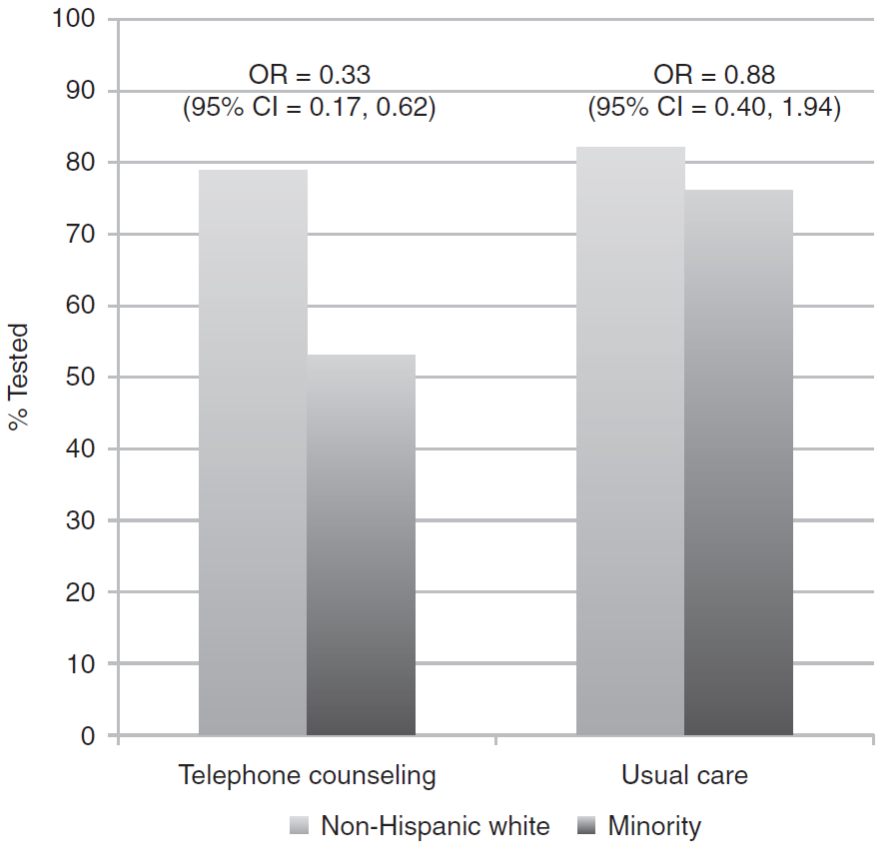


Figure 2 Race by group interaction in intention-to-treat sample.

Butrick et al., 2015

HBOC Population Screening Tradeoffs for Communities of African Ancestry

Benefits

- Women of AAn > advanced disease and > mortality
- Women of AAn > likelihood for mutations
- At risk family members can benefit
- Mutations inform risk for other cancers

Limitations

- Healthy individuals with information
  - Increased anxiety & existential concerns
  - More likely to have VUS
  - No clear treatment course
  - Family members diffusion
- 85-95% will not be at risk
  - Misunderstanding

ACR recommends all women of AAn be screened for breast cancer risk < 30

GEORGIA BREAST CANCER GENOMIC CONSORTIUM

EDUCATION SURVEILLANCE AND POLICY

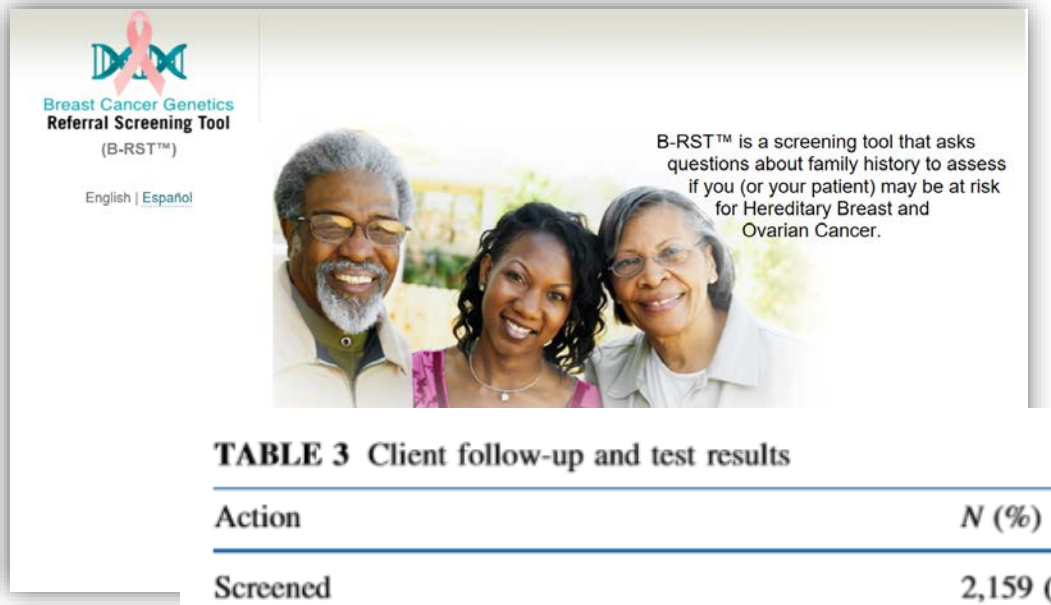


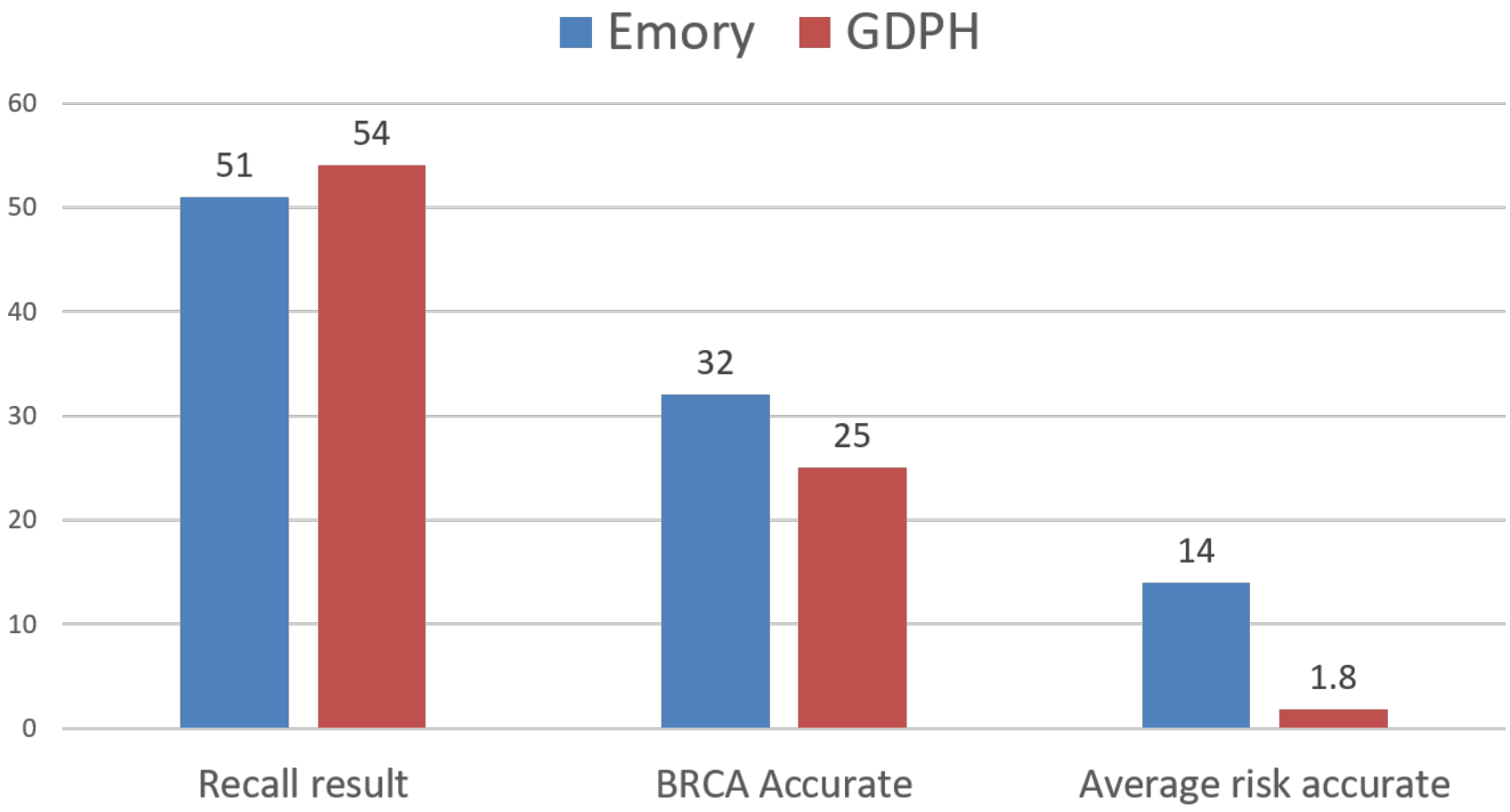
TABLE 3 Client follow-up and test results

Action	*N* (%)
Screened	2,159 (100)
Positive screens	130 (6.0)
Agreed to follow-up	110 (84.6)
Successfully contacted for follow-up	67 (60.9)
Met NCCN guidelines for testing	47 (65.7)
Underwent genetic testing	14 (29.8)
Genetic variants	2 (14.3)
BRCA2 mutation	1 (7.1)
Variant of uncertain significance	1 (7.1)

- **Ongoing in 13 districts**
- **Approached in women's health clinics; ages 25-49**
- **Nov 2012 - Dec 2013 screened 2,159 women** (3% of eligible patients)
- **Majority of patients AA**

Traxler et al., Ann Surg Oncol, 2014

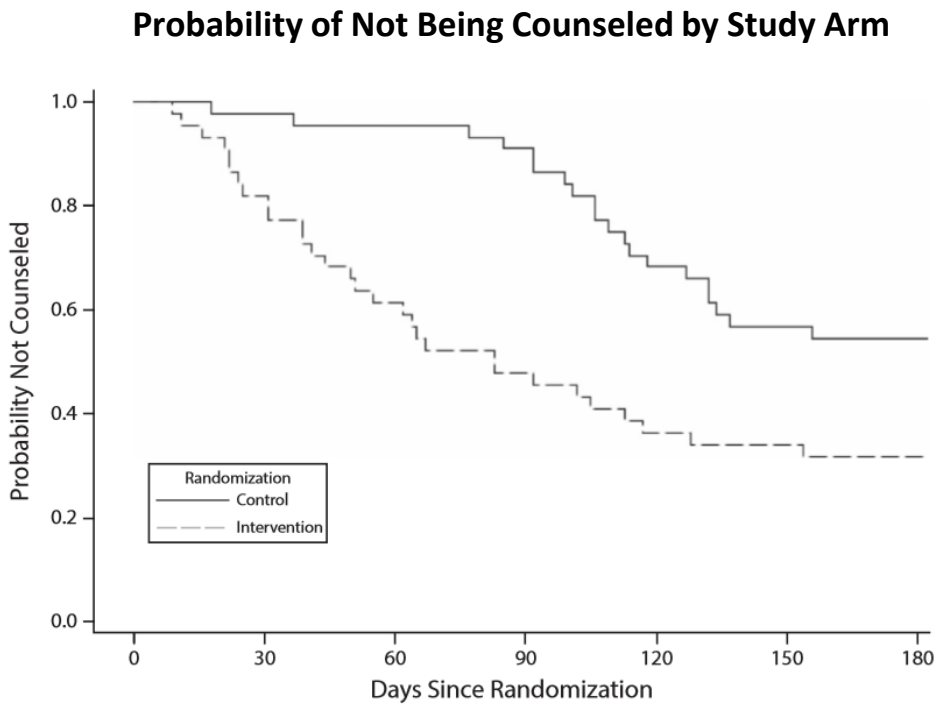
Understanding of BRST results among those with negative results: Georgia Experience



Guan Y et al., in preparation

Mismatch of Genetic Counseling Audiences with Low Literacy

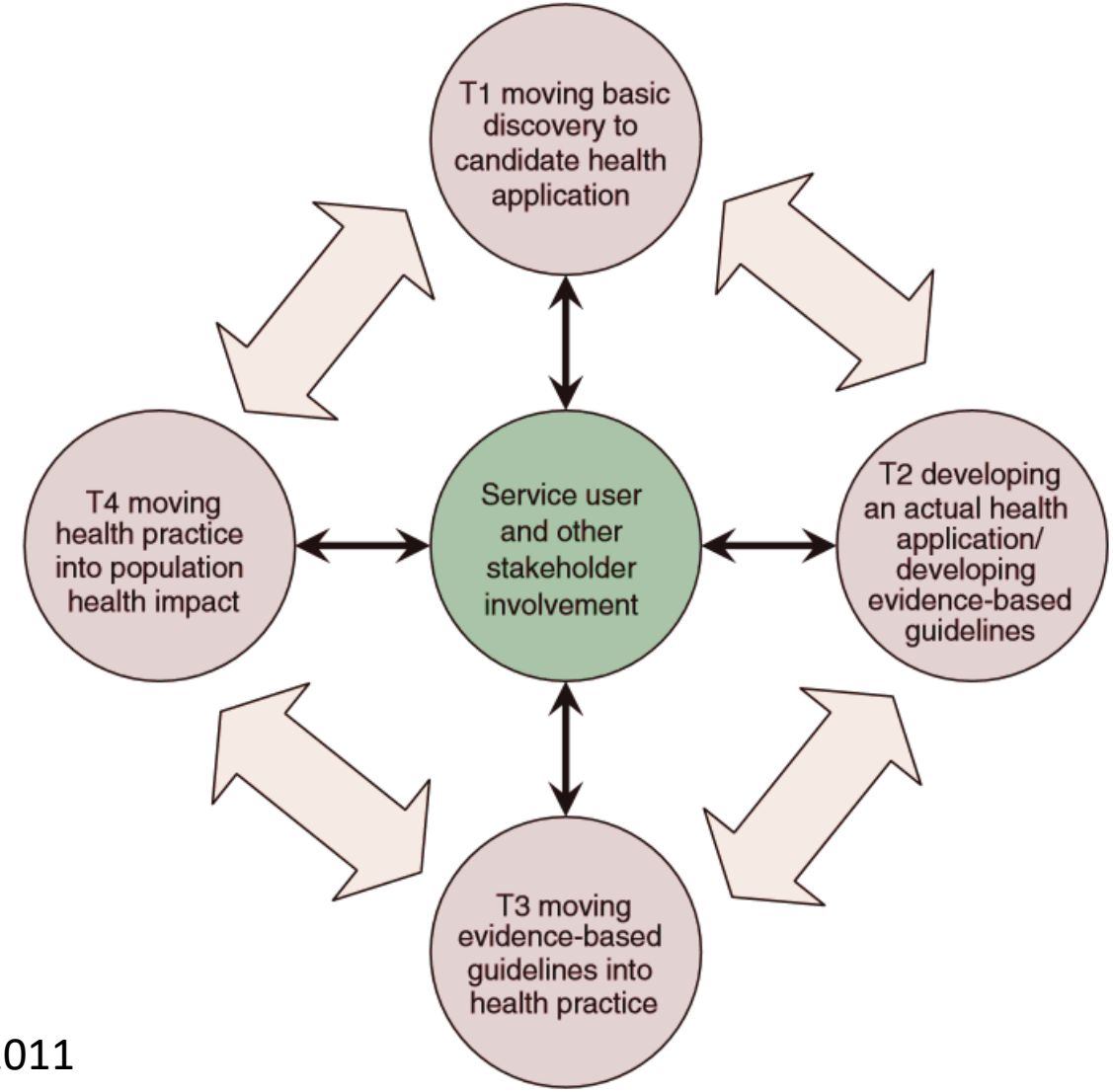
- **English, Spanish, Chinese-speakin (N=124)**
- **170 genetic coun appointments**
- **Mismatch**
  - Too much informati
  - Complex terminolo
  - Information not per relevant
  - Unintentional inhibi patient engagemen
  - Vague descriptions prevention



Joseph et al., 2017; Pasick, Joseph et al, 2016

BRIDGING THE TRANSLATION GAP

Envisoning (Post)Genomic Translation Research as an Interlocking Loop



Callard et al., 2011

Scientific Inclusion

- **Appropriate reach of "precision public health"**
  - Uptake individuals & families
  - Outside of clinical settings
  - SBC challenges intersect with basic science, epidemiology & clinical
- **Averting disparities, an opportunity for interdisciplinary collaborations**
  - Problem-based discussions
  - National forums needed to foster cross disciplinary conversations
  - Must include community partners
- **Need incentives for collaboration**
  - NIH and other funders to incentivize interdisciplinary collaborations

Genomics to reduce disparities recommendations

- Minority-focused genetic research
  - Framing basic science research benefits to minority communities
- Community-based participatory research
  - Bring novel engagement approaches to the table
- GxE Research aligned with social determinants of health -- epigenetics
  - Study health issues of concern to communities
- Public education
  - Clinical settings
  - Community settings

Smith et al., Health Affairs, 2016
Landry et al., 2018

THANK YOU!